BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images, please do not report the images to the Image Problem Mailbox.

RESPONSE UNDER 37 C.F.R.
EXPEDITED PROCEDURE
EXAMINING GROUP

In the Claims

Please amend claims 7, 9, 10, 13, 14 and 16 to read as follows.

D1

7. (Twice amended) A compound according to Claim ~~16~~ 1 in which Ar^2 is a 1,4-phenylene group optionally substituted with one or two atoms or groups $-L^2(Alk)_tL^3(R^4)_u$.

D2

9. (Twice amended) A compound according to Claim 16 in which Ar^1 is a pyrimidinyl, pyridyl or phenyl group optionally substituted with one or more atoms or groups $-L^2(Alk)_tL^3(R^4)_u$.

10. (Amended) A compound according to Claim 9 in which Ar^1 is a pyridyl or phenyl group optionally substituted with one or more atoms or groups $-L^2(Alk)_tL^3(R^4)_u$.

D3

13. (Amended) A compound according to Claim 12 in which R^3 is a pyrrolidinyl or thiazolidinyl group optionally substituted with one or more halogen atoms, C_{1-6}alkyl groups, haloC_{1-6}alkyl groups optionally substituted with one or more hydroxyl groups, hydroxyl groups, C_{1-6}alkoxy groups, haloC_{1-6}alkoxy groups, thiol groups, C_{1-6}alkylthio groups, aromatic groups, heteroaromatic groups, or $-(Alk^2)_vR^{10}$ groups, and each nitrogen atom of the pyrrolidinyl or thiazolidinyl group is optionally substituted with a group $-(L^5)_p(Alk^3)_qR^{12}$;

or R^3 is a phenyl, pyrimidinyl or 1,3,5-triazinyl group optionally substituted with one or more atoms or groups $-R^{13a}$ or $-Alk^4(R^{13a})_m$.

D3

14. (Amended) A compound which is:

3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-3-({4-[2-hydroxyethylamino]-6-methoxy-1,3,5-triazin-2-yl}amine)propanoic acid;

3-[(3,5-Dichloroisonicotinoyl)amino]-3-{4-[(3,5-dichloroisonicotinoyl)-amino]phenyl}propanoic acid;

3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-3-[(2,6-dimethoxybenzoyl)amino]propanoic acid;

3-({[(4S)-3-Acetyl-1,3-thiazolinan-4-yl]carbonyl}amino-3-{4-[(3,5-dichloroisonicotinoyl)amino]phenyl}propanoic acid;

3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-3-[({(2S)-1-[(3,5-dichlorophenyl)sulphonyl]tetrahydro-1-H-pyrrol-2-yl}carbonyl)amino]propanoic acid;

(2*RS*,3*RS*)-3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-3-{[(2S)-1-[(3,5-dichlorophenyl)sulphonyl]tetrahydro-1-H-pyrrol-2-yl)carbonyl]amino}-2-hydroxypropanoic acid;

3-{4-[(3,5-Dichloroisonicotinoyl)amino]phenyl}-3-[({2-[(2,5-dimethoxyphenyl)thio]-3-pyridinyl}carbonyl)amino]propanoic acid;

and the salts, hydrates and N-oxides thereof.

16. (Amended three times) A compound of formula (1):

$$Ar^1(Alk^a)_rL^1Ar^2CH(R^1)C(R^a)(R^{a'})R \qquad (1)$$

wherein

Ar^1 is an aromatic or C_{1-9} heteroaromatic group containing one to four heteroatoms seleted from oxygen, nitrogen, and sulfur, and is optionally substituted with one or more atoms or groups $-L^2(Alk)_tL^3(R^4)_u$;

L^2 and L^3, which may be the same or different, is each a covalent bond or a divalent linker atom or group selected from -O-, -S-, -C(O)-, -C(O)O-, -OC(O)-, -C(S)-, -S(O)-, $-S(O)_2-$, $-N(R^8)-$, $-CON(R^8)-$, $-OC(O)N(R^8)-$, $-CSN(R^8)-$, $-N(R^8)CO-$, $-N(R^8)C(O)O-$, $-N(R^8)CS-$, $-S(O)_2N(R^8)-$, $-N(R^8)S(O)_2-$, $-N(R^8)CON(R^8)-$, $-N(R^8)CSN(R^8)-$, and $-N(R^8)SO_2N(R^8)-$;

R^8 is a hydrogen atom or a C_{1-6}alkyl group optionally substituted with one or more halogen atoms, hydroxy groups, or C_{1-6}alkoxy groups;

t is zero or the integer 1;

u is an integer 1, 2 or 3;

Alk is an aliphatic or heteroaliphatic chain;

R^4 is a hydrogen or halogen atom or a group selected from C_{1-6}alkyl, $-OR^5$, $-SR^5$, $-NR^5R^6$, $-NO_2$, -CN, $-CO_2R^5$, $-SO_3H$, $-SO_3R^5$, $-SOR^5$, $-SO_2R^5$, $-OCO_2R^5$, $-CONR^5R^6$,

-OCONR^{5}R^6, -CSNR^{5}R^6, -COR^5, -OCOR^5, -N(R^5)COR^6, -N(R^5)CSR^6, -SO$_2$N(R^5)(R^6), -N(R^5)SO$_2$R^6, -N(R^5)CON(R^6)(R^7), -N(R^5)CSN(R^6)(R^7), and -N(R^5)SO$_2$N(R^6)(R^7); and

04

R^5, R^6, and R^7, which may be the same or different, is each a hydrogen atom or a straight or branched C$_{1-6}$alkyl group optionally substituted with one or more halogen atoms, hydroxy groups, or C$_{1-6}$alkoxy groups;

provided that when t is zero and each of L^2 and L^3 is a covalent bond, then u is the integer 1 and R^4 is other than a hydrogen atom;

L^1 is a covalent bond or a linker atom or group selected from -CON(R^2)-, -S(O)$_2$N(R^2)-, -N(R^2)-, and -O-;

R^2 is a hydrogen atom or a C$_{1-3}$ alkyl group;

Ar^2 is a phenylene group optionally substituted with one or two atoms or groups -L^2(Alk)$_t$L^3(R^4)$_u$;

R^1 is a group selected from -NHCOR^3, -NHSO$_2$R^3, -NHR^3, -NHC(O)OR^3, -NHCSR^3, -NHCON(R^3)(R^{3a}), -NHSO$_2$N(R^3)(R^{3a}), and -NHCSN(R^3)(R^{3a});

R^3 is an optionally substituted C$_{3-10}$ cycloaliphatic group, an optionally substituted C$_{7-10}$ polycycloaliphatic group, an optionally substituted C$_{3-10}$ heterocycloaliphatic group containing one, two, three or four heteroatoms or heteroatom-containing groups selected from -O-, -S-, -C(O)-, -C(O)O-, OC(O)-, -C(S)-, -S(O)-, -S(O)$_2$-, -N(R^8)-, -C(O)NR^8-, -OC(O)N(R^8)-, -CSN(R^8)-, -N(R^8)CO-, -N(R^8)C(O)O-, -N(R^8)CS-, -S(O)$_2$N(R^8)-, -N(R^8)S(O)$_2$-,

$-N(R^8)CON(R^8)-$, $-N(R^8)CSN(R^8)-$ and $-N(R^8)SO_2N(R^8)-$; an optionally substituted C_{7-10} heteropolycycloaliphatic group containing one, two, three or four heteroatoms or heteroatom-containing groups selected from -O-, -S-, -C(O)-, -C(O)O-, OC(O)-, -C(S)-, -S(O)-, $-S(O)_2-$, $-N(R^8)-$, $-C(O)NR^8-$, $-OC(O)N(R^8)-$, $-CSN(R^8)-$, $-N(R^8)CO-$, $-N(R^8)C(O)O-$, $-N(R^8)CS-$, $-S(O)_2N(R^8)-$, $-N(R^8)S(O)_2-$, $-N(R^8)CON(R^8)-$, $-N(R^8)CSN(R^8)-$ and $-N(R^8)SO_2N(R^8)-$; an optionally substituted aromatic group, or an optionally substituted C_{1-9} heteroaromatic group containing one, two, three or four heteroatoms seleted from oxygen, nitrogen, and sulfur;

R^{3a} is a hydrogen atom, an optionally substituted C_{1-6} aliphatic group, an optionally substituted C_{1-6} heteroaliphatic group containing one, two, three or four heteroatoms or heteroatom-containing groups selected from -O-, -S-, -C(O)-, -C(O)O-, OC(O)-, -C(S)-, -S(O)-, $-S(O)_2-$, $-N(R^8)-$, $-C(O)NR^8-$, $-OC(O)N(R^8)-$, $-CSN(R^8)-$, $-N(R^8)CO-$, $-N(R^8)C(O)O-$, $-N(R^8)CS-$, $-S(O)_2N(R^8)-$, $-N(R^8)S(O)_2-$, $-N(R^8)CON(R^8)-$, $-N(R^8)CSN(R^8)-$ and $-N(R^8)SO_2N(R^8)-$, an optionally substituted C_{3-10} cycloaliphatic group, an optionally substituted C_{7-10} polycycloaliphatic group, an optionally substituted C_{3-10} heterocycloaliphatic group containing one, two, three or four heteroatoms or heteroatom-containing groups selected from -O-, -S-, -C(O)-, -C(O)O-, OC(O)-, -C(S)-, -S(O)-, $-S(O)_2-$, $-N(R^8)-$, $-C(O)NR^8-$, $-OC(O)N(R^8)-$, $-CSN(R^8)-$, $-N(R^8)CO-$, $-N(R^8)C(O)O-$, $-N(R^8)CS-$, $-S(O)_2N(R^8)-$, $-N(R^8)S(O)_2-$, $-N(R^8)CON(R^8)-$, $-N(R^8)CSN(R^8)-$ and $-N(R^8)SO_2N(R^8)-$; an optionally substituted C_{7-10} heteropolycycloaliphatic group containing one, two, three or four heteroatoms or heteroatom-containing groups selected from -O-, -S-, -C(O)-, -C(O)O-, OC(O)-, -C(S)-, -S(O)-, $-S(O)_2-$,

66

D

-N(R^8)-, -C(O)NR^8-, -OC(O)N(R^8)-, -CSN(R^8)-, -N(R^8)CO-, -N(R^8)C(O)O-, -N(R^8)CS-, -S(O)$_2$N(R^8)-, -N(R^8)S(O)$_2$-, -N(R^8)CON(R^8)-, -N(R^8)CSN(R^8)- and -N(R^8)SO$_2$N(R^8)-; an optionally substituted aromatic group, or an optionally substituted C_{1-9} heteroaromatic group containing one, two, three or four heteroatoms seleted from oxygen, nitrogen, and sulfur;

wherein the optional substituents for the aromatic groups and the heteroaromatic groups of R^3 and R^{3a} are selected from one or more atoms or groups R^{13} wherein R^{13} is -R^{13a} or -Alk^4(R^{13a})$_m$;

R^{13a} is a halogen atom, or an amino, substituted amino, nitro, cyano, amidino, hydroxyl, substituted hydroxyl, formyl, carboxyl, esterified carboxyl, thiol, substituted thiol, -COR^{14}; -CSR^{14}, -SO$_3$H, -SOR^{14}, -SO$_2$R^{14}, -SO$_2$NH$_2$, -SO$_2$NHR^{14}, -SO$_2$N(R^{14})$_2$, -CONH$_2$, -CSNH$_2$, -CONHR^{14}, -CSNHR^{14}, -CON(R^{14})$_2$, -CSN(R^{14})$_2$, -N(R^{11})SO$_2$R^{14}, -N(SO$_2$R^{14})$_2$, -N(R^{11})SO$_2$NH$_2$, -N(R^{11})SO$_2$NHR^{14}, -N(R^{11})SO$_2$N(R^{14})$_2$, -N(R^{11})COR^{14}, -N(R^{11})CONH$_2$, -N(R^{11})CONHR^{14}, -N(R^{11})CON(R^{14})$_2$, -N(R^{11})CSNH$_2$, -N(R^{11})CSNHR^{14}, -N(R^{11})CSN(R^{14})$_2$, -N(R^{11})CSR^{14}, -N(R^{11})C(O)OR^{14}, -SO$_2$NHet^1, -CONHet^1, -CSNHet^1, -N(R^{11})SO$_2$NHet^1, -N(R^{11})CONHet^1, -N(R^{11})CSNHet^1, -SO$_2$N(R^{11})Het^2, -Het^2, -CON(R^{11})Het^2, -CSN(R^{11})Het^2, -N(R^{11})CON(R^{11})Het^2, -N(R^{11})CSN(R^{11})Het^2, aryl or heteroaryl group;

R^{14} is an -Alk^4(R^{13a})$_m$, aryl or heteroaryl group;

NHet^1 is a C_{5-7}cyclicamino group optionally containing one or more -O- or -S- atoms or -N(R^{11})-, -C(O)- or -C(S)- groups and optionally substituted with one or more substituents as defined for the cycloaliphatic groups of R^3 and R^{3a};

Het^2 is a monocyclic C_{5-7}carbocyclic group optionally containing one or more -O- or -S- atoms or $-N(R^{11})-$, -C(O) or -C(S)- groups and optionally substituted with one or more substituents as defined for the cycloaliphatic groups of R^3 and R^{3a};

Alk^4 is a straight or branched C_{1-6}alkylene, C_{2-6}alkenylene or C_{2-6}alkynylene chain, optionally interrupted by one, two, or three -O- or -S- atoms or $-S(O)_n$ or $-N(R^{15})-$ groups;

R^{15} is a hydrogen atom or C_{1-6}alkyl group;

m is zero or an integer 1, 2 or 3;

n is an integer 1 or 2;

wherein the optional substituents for the aliphatic groups and the heteroaliphatic groups of R^{3a} are selected from halogen atoms, hydroxy groups, C_{1-6}alkoxy groups, thiol groups, C_{1-6}alkylthio groups, amino groups, and substituted amino groups;

wherein the optional substituents for the cycloaliphatic, polycycloaliphatic, heterocycloaliphatic and heteropolycycloaliphatic groups of R^3 and R^{3a} are selected from halogen atoms, C_{1-6}alkyl groups, haloC_{1-6}alkyl groups optionally substituted with hydroxyl groups, hydroxyl groups, C_{1-6}alkoxy groups, haloC_{1-6}alkoxy groups, thiol groups, C_{1-6}alkylthio groups, aromatic groups, heteroaromatic groups, and $-(Alk^2)_vR^{10}$ groups;

Alk^2 is a straight or branched C_{1-3} alkylene chain;

v is zero or an integer 1;

R^{10} is a -OH, -SH, $-N(R^{11})_2$, -CN, $-CO_2R^{11}$, $-NO_2$, $-CON(R^{11})_2$, $-CSN(R^{11})_2$, $-OC(O)N(R^{11})_2$, -C(O)H, $-COR^{11}$,$-OCO_2R^{11}$, $-OC(O)R^{11}$, $-C(S)R^{11}$, $-CSN(R^{11})_2$, $-N(R^{11})COR^{11}$,

$-N(R^{11})CSR^{11}$, $-SO_3H$, $-SOR^{11}$, $-SO_2R^{11}$, $-SO_3R^{11}$, $-SO_2N(R^{11})_2$, $-N(R^{11})SO_2R^{11}$, $-N(R^{11})CON(R^{11})_2$, $-N(R^{11})CSN(R^{11})_2$, or $-N(R^{11})SO_2N(R^{11})_2$ group; and

R^{11} is an atom or group as defined for R^8 or an optionally substituted cycloaliphatic or hetercycloaliphatic group as defined for R^3;

and when R^3 is a heterocycloaliphatic group containing one or more nitrogen atoms each nitrogen atom is optionally substituted with a group $-(L^5)_p(Alk^3)_qR^{12}$;

L^5 is -C(O)-, -C(O)O-, -C(S)-, -S(O)-, $-S(O)_2-$, $-CON(R^{11})-$, $-CSN(R^{11})-$, $-SON(R^{11})-$ or $-SO_2N(R^{11})-$;

p is zero or an integer 1;

Alk^3 is an optionally substituted aliphatic or heteroaliphatic chain;

q is zero or an integer 1;

R^{12} is a hydrogen atom or an optionally substituted cycloaliphatic, heterocycloaliphatic, polycycloaliphatic, polyheterocycloaliphatic, aromatic or heteroaromatic group;

R^a and $R^{a'}$, which may be the same or different, are each independently selected from a hydrogen or halogen atom or an optionally substituted straight or branched alkyl, alkenyl, alkynyl, haloalkyl, alkoxy, haloalkoxy, alkylthio or $-(Alk^b)_mR^b$ group (in which Alk^b is a C_{1-3} alkylene chain, m is zero or the integer 1, and R^b is -OH, -SH, $-NO_2$, -CN, $-CO_2H$, $-CO_2R^c$ (where R^c is an optionally substituted straight or branched C_{1-6} alkyl group), $-SO_3H$, $-SOR^c$, $-SO_2R^c$, $-SO_3R^c$, $-OCO_2R^c$, -C(O)H, $-C(O)R^c$, $-OC(O)R^c$, $-C(S)R^c$, $-NR^dR^e$ (where R^d and R^e, which may

be the same or different, are each a hydrogen atom or an optionally substituted straight or branched C_{1-6} alkyl group), $-CON(R^d)(R^e)$, $-OC(O)N(R^d)(R^e)$, $-N(R^d)C(O)R^e$, $-CSN(R^d)(R^e)$, $-N(R^d)C(S)R^e$, $-S(O)_2N(R^d)(R^e)$, $-N(R^d)SO_2R^e$, $-N(R^d)CON(R^e)(R^f)$ (where R^f is a hydrogen atom or an optionally substituted straight or branched C_{1-6} alkyl group), $-N(R^d)C(S)N(R^e)(R^f)$ or $-N(R^d)SO_2N(R^e)(R^f)$ group);

Alk^a is an optionally substituted C_{1-6} aliphatic or C_{1-6} heteroaliphatic chain containing one, two, three or four heteroatoms or heteroatom-containing groups selected from -O-, -S-, -C(O)-, -C(O)O-, OC(O)-, -C(S)-, -S(O)-, $-S(O)_2-$, $-N(R^8)-$, $-C(O)NR^8-$, $-OC(O)N(R^8)-$, $-CSN(R^8)-$, $-N(R^8)CO-$, $-N(R^8)C(O)O-$, $-N(R^8)CS-$, $-S(O)_2N(R^8)-$, $-N(R^8)S(O)_2-$, $-N(R^8)CON(R^8)-$, $-N(R^8)CSN(R^8)-$, and $-N(R^8)SO_2N(R^8)-$;

wherein the optional substituents for the aliphatic and heteroaliphatic groups of Alk^a are selected from halogen atoms, hydroxy groups, C_{1-6}alkoxy groups, thiol groups, C_{1-6}alkylthio groups, amino groups, and substituted amino groups;

r is zero or the integer 1;

R is a carboxylic acid (CO_2H), a carboxylic ester group, or carboxylic amide group;

and the salts, hydrates and N-oxides thereof.

17. (Twice amended) A method for the treatment of a mammal suffering from inflammatory arthritis, multiple sclerosis, allograft rejection, diabetes, inflammatory dermatoses, asthma or